IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

UNITED STATES OF AMERICA, Plaintiff, v. BAYER CORPORATION Defendant.	Case No. 2:07-cv-00001-JLL-JAD (Hon. Jose L. Linares) (Hon. Joseph A. Dickson) *Document Filed Electronically*

BRIEF OF AMICUS CURIAE COUNCIL FOR RESPONSIBLE NUTRITION

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INTEREST OF THE COUNCIL FOR RESPONSIBLE NUTRITION

Amicus curiae the Council for Responsible Nutrition ("CRN") is the leading trade association for the dietary supplement industry, representing manufacturers of dietary ingredients and of national brand name and private label dietary supplements. CRN represents more than 150 companies worldwide that manufacture and market dietary ingredients or dietary supplements, or supply services to those suppliers and manufacturers. CRN members manufacture popular national brands, as well as the store brands marketed by major supermarket, drug store, and discount chains. These products also include those marketed through natural food stores and mainstream direct selling companies.

CRN submitted a brief of *amicus curiae* on October 3, 2014 ("CRN's October *Amicus* Brief") which included a comprehensive discussion of CRN's interest in the case. Dkt. No. 24-2. The Court granted CRN's motion for leave to file a brief of *amicus curiae* on October 23, 2014, finding that the *amici* briefs of CRN and another dietary supplement industry trade association were informative "and of assistance to the Court, particularly in considering the implications of the ultimate outcome of this dispute on the entire dietary supplement industry." Dkt. No. 47 at 3-4. The Court's Order dated November 3, 2014 provides for the submission of addition *amicus* briefs by CRN and the other trade association by March 17, 2015. Dkt. No. 53. CRN appreciates this opportunity to provide further

insight into the implications for the whole industry now that discovery obtained since the submission of CRN's October *Amicus* Brief has confirmed that the evidentiary standard the government seeks to apply in this case would be extended to all dietary supplements.

Given the broad scope of CRN membership and CRN's deep involvement with the development of the law establishing the regulatory regime specific to dietary supplements – the Dietary Supplement Health and Education Act of 1994 ("DSHEA"), Pub. L. No. 103-417, 108 Stat. 4325 (1994) – CRN believes it offers an important perspective to the Court as it considers the merits of this case. CRN does not take a position on any scientific or factual issues in this matter. Rather, CRN continues to have a special interest in this case because what is at issue is the appropriate standard for substantiating non-disease claims made for dietary supplements.

The government's proffered standard, articulated by its expert, gastroenterologist Dr. Loren Laine, and expounded upon in his deposition testimony filed after the submission of CRN's October *Amicus* Brief, closely resembles the evidentiary standard for the approval of new drugs – a standard that was firmly rejected by Congress for dietary supplements and which reflects a significant departure from longstanding Federal Trade Commission ("FTC") and

U.S. Food and Drug Administration ("FDA") guidance and precedent upon which the supplement industry has long relied.

While the government asserted in its Response to CRN's October *Amicus* Brief that this matter is solely about determining whether Bayer Corporation ("Bayer") possessed competent and reliable scientific evidence for its particular digestive health benefit claims for its Phillips Colon Health ("PCH") product and is not of relevance to the broader industry, Dkt. No. 40 at 1, the government's expert, Dr. Laine, testified in his deposition that his evidentiary standard would apply to all dietary supplements. Dkt. No. 73-2. Even more concerning to CRN is that Dr. Laine addressed a number of marketed probiotic supplement products, some of which are produced by CRN members, and asserted that his standard would apply to all of the digestive health benefit claims made on those products that were similar to those made for Bayer's PCH. This testimony, as well as other discovery in the case, therefore reveals that, in fact, this case *is* about the appropriate evidentiary standard for non-disease health benefit claims for dietary supplements in general, and for digestive health benefit claims for probiotic supplements in particular. CRN and its members therefore continue to have a strong interest in this case.

SUMMARY OF ARGUMENT

In this case, the government is attempting to impose a standard equivalent to that required for new drug approval to the substantiation of dietary supplement claims that do not relate to the prevention or treatment of disease. The government's expert in this case, Dr. Laine, testified that his evidentiary standard would apply equally to dietary supplements and drugs, as well as to physical therapy, dietary modifications, or anything else that may be the subject of clinical research. This across-the-board standard would be inordinately expensive and unduly burdensome on the dietary supplement industry, and imposing this standard would deny consumers access to scientifically valid information about the health benefits of dietary supplements. Further, such a drug-like evidentiary standard would wholly undermine the regulatory scheme established by Congress through the enactment of DSHEA, which created a new regime for the regulation of dietary supplements that is distinct from the regulation of drug products.

The government's rigid substantiation standard asserted in this case is novel and a grave departure from the longstanding "competent and reliable scientific evidence" standard upon which the dietary supplement industry has relied for decades. As discussed in detail in CRN's October *Amicus* brief, both the FTC and FDA have long insisted that the "competent and reliable scientific evidence" standard is flexible and that there is no fixed formula as to the number or type of

studies needed to support health benefit claims (unless the claim states that it is supported by a specific amount or type of evidence). Yet here, the government would insist on a highly-specific, multi-part test for substantiation that would apply equally to all dietary supplements, drugs, and other interventions that are the subject of clinical research.

Discovery obtained since the submission of CRN's October *Amicus* Brief has only confirmed that the evidentiary standard the government seeks to apply in this case would be extended to all dietary supplements. Specifically, the government expert's testimony that his rigid and allegedly rigorous standard would apply to all dietary supplement claims stands in direct contrast to the government's insistence, in its response to CRN's October *Amicus* Brief, that this case is solely about Bayer's substantiation for its specific claims for PCH and is not about legal standards for the broader dietary supplement industry. Dkt. No. 40 at 1. Moreover, as detailed below, the government's responses to discovery requests in this case, both of which were served after the submission of CRN's October *Amicus* brief, reveal an attempt to suggest that the FTC has long put the industry on notice that randomized, controlled clinical trials ("RCTs") are required for a broad range of health benefit claims. Government's Response to Defendant's First Request for Interrogatories, Dkt. No. 73-9; Government's Amended Response to Defendant's First Requests for Admission, Dkt. No. 73-8.

The government's approach, as articulated in these discovery responses and in Dr. Laine's deposition, makes no sense, and creates great confusion for the dietary supplement industry. The government seeks to have it both ways – it insists that the instant case is only about the evidence Bayer needs to substantiate its particular claims for PCH and that the FTC retains its longstanding flexible standard as a general matter, while also asserting that the FTC has long required RCTs for a broad, undefined category of claims such that the industry should have been on notice that RCTs are required. Effectively, the government is saying that the FTC has a flexible substantiation standard under which a dietary supplement marketer might need RCTs to support its non-disease claims, but it might not, and the company will not know which is the case until it becomes the subject of an enforcement action and learns what the FTC's particular expert in the case wants to see. Such a lack of clear and consistent guidance is untenable for the regulated industry and creates a chilling effect on the communication of truthful, valuable, and scientifically sound information about dietary supplements out of fear of enforcement action. Consumers would thereby be denied access to information about the health benefits of certain dietary supplements and would not be able to make fully informed nutrition-related decisions. Such an outcome is precisely what DSHEA was designed to avoid.

ARGUMENT

I. The Government Seeks to Impose an Evidentiary Standard for Dietary Supplements That Was Rejected by Congress and Conflicts With Longstanding FTC and FDA Precedent

A. DSHEA and FTC and FDA Guidance Reject a Broad Requirement for RCTs for Non-Disease Claims for Dietary Supplements

As discussed extensively in CRN's October *Amicus* Brief, DSHEA amended the Federal Food, Drug, and Cosmetic Act to create a new regime for FDA's regulation of dietary supplements that is distinct from FDA's regulation of drug products. In enacting DSHEA, Congress aimed to "assure citizens have continued access to dietary supplements and information about their benefits." S. Rep. No. 103-410, at 17 (1994). Congress made clear in DSHEA that "there is a growing need for emphasis on the dissemination of information linking nutrition and long-term good health," that "consumers should be empowered to make choices about preventive health care programs based on data from scientific studies of health benefits related to particular dietary supplements," and that "the Federal Government should not take any actions to impose unreasonable regulatory barriers limiting or slowing the flow of safe products . . . to consumers." DSHEA, § 2(7), (8), (13).

Since DSHEA's enactment in 1994, both the FTC and FDA have issued guidance documents for the dietary supplement industry that describe the amount, type, and quality of evidence that dietary supplement manufacturers should have in

order to substantiate that a claim made about a dietary supplement is truthful and not misleading. *See* FTC, *Dietary Supplements: An Advertising Guide for Industry* (Apr. 2001), *available at* http://www.ftc.gov/system/files/documents/plain-language/bus09-dietary-supplements-advertising-guide-industry.pdf ("FTC Guidance"); FDA, *Guidance for Industry: Substantiation for Dietary Supplement Claims Made Under Section 403(r)(6) of the Federal Food, Drug, and Cosmetic Act* (Dec. 2008), *available at* http://www.fda.gov/food/guidanceregulation/guidancedocumentsregulatoryinformation/ucm073200.htm ("FDA Guidance").

These guidance documents are the only publications through which the FTC and FDA have communicated, broadly, to the entire industry, current agency thinking regarding the evidence necessary to substantiate non-disease claims made about dietary supplements. The dietary supplement industry thus has relied heavily for many years on these guidance documents in evaluating whether there is adequate evidence to substantiate a given non-disease claim.

Both guidance documents establish that health benefit claims for dietary supplements must be substantiated by "competent and reliable scientific evidence," which is defined as:

> tests, analyses, research, studies, or other evidence based on the expertise of professionals in the relevant area, that have been conducted and evaluated in an objective manner by persons qualified to do so, using procedures

> generally accepted in the profession to yield accurate and reliable results.

See, e.g., FTC Guidance at 9. Both the FTC and FDA guidance documents clearly communicate that there is "*no fixed formula* for the number or type of studies required" to substantiate a health benefit claim. FTC Guidance at 9 (emphasis added); *see also* FDA Guidance ("*there is no pre-established formula* as to how many or what type of studies are needed to substantiate a claim . . .") (emphasis added). Further, both guidance documents identify a range of evidence that could help provide competent and reliable scientific evidence in support of a health benefit claim, including animal and *in vitro* studies, research explaining the biological mechanism underlying the claimed effect, and epidemiological evidence. *See* FTC Guidance at 10; FDA Guidance. Finally, the FTC acknowledges that advertisers may consider whether it may be appropriate to "extrapolate from the research to the claimed effect," FTC Guidance at 16, and provides that in certain circumstances it could be "scientifically sound to make such extrapolations." *Id*. at 17.

B. The Government Would Impose a New, Rigid RCT Requirement for Non-Disease Claims for Dietary Supplements

Bayer is subject to an FTC consent order that requires it to possess "competent and reliable scientific evidence" for its dietary supplement claims; as the government has recognized, that term is defined in the consent order identically

to how it is defined in FTC's guidance (except for a typographical error). In the instant case, the government asserts that Bayer did not possess competent and reliable scientific evidence for certain non-disease claims about its PCH product, including express claims to "promote overall digestive health," to help "defend against occasional constipation, diarrhea, gas and bloating," and to "help with occasional constipation, diarrhea, gas and bloating." Dkt. No. 4 at 5-6, 9-10. As detailed in CRN's October *Amicus* Brief, these claims are squarely within those FDA has long accepted as lawful non-disease claims for dietary supplements. Dkt. No. 24-2 at 11.

The government further asserts that Bayer impliedly claims that PCH prevents, cures, or treats constipation, diarrhea, and gas and bloating. Even if Bayer does make such claims, they should not be subject to the drug-like substantiation standard the government asserts. It is well-established that a product can be intended to treat a symptom without being intended to treat a disease. For example, in the preamble to FDA's final rule for structure/function claims for dietary supplements, FDA made clear that claims about symptoms that are not characteristic of diseases are structure/function claims, not drug claims. Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body, 65 Fed. Reg. 1000, 1031 (Jan. 6, 2000). In doing so, FDA expressly addressed claims to alleviate gas, bloating, and

occasional constipation, and concluded that these are structure/function claims, not disease (drug) claims. *Id*. Through this case, the government is attempting to impose a drug-like substantiation standard on claims that are *not* drug claims, but are rather lawful structure/function claims that are being made about a dietary supplement product.

The government's expert gastroenterologist, Dr. Laine, opined that competent and reliable scientific evidence for Bayer's PCH claims "requires human clinical trials that (1) are randomized, placebo-controlled, and double-blind; (2) use the specific product [including the specific probiotic strains] for which the claims are made; [and] (3) are performed in the population at which the claims are directed." Dkt. No. 4 at 16; *see also* Dkt. No. 73-2 (Laine Deposition) at 16:4-6, 22; 17:2, 11, 18-19; 18:13-15.

The government asserts more specifically that, "for a study to serve as competent and reliable scientific evidence to substantiate, for example, a claim that a product helps defend against a specific symptom," the study must be conducted on a symptom-free population. Dkt. No. 4 at 24; *see also* Dkt. No. 73-2 at 24:11-13. The government further alleges that if a manufacturer's substantiation does not contain "all of the required elements," Dkt. No. 4 at 24, it cannot be competent and reliable scientific evidence. The "required elements" that the government identifies in its motion and that Dr. Laine further explained in his deposition are

not enumerated in any statutory provision or agency guidance related to non-disease claims about dietary supplements, but rather are those desired by the government's expert in this enforcement proceeding. Through this action, the government is effectively attempting to redefine "competent and reliable scientific evidence."

These "required elements" represent a significant departure from the flexibility set forth in the FTC and FDA Guidance upon which the dietary supplement industry has relied for many years. Further, imposing these "required elements" for *non-disease* claims for dietary supplements would exceed substantiation requirements that courts have recently recognized as reasonable for FTC to impose for *disease* claims. Most recently, the D.C. Circuit considered whether an FTC order requiring two RCTs to substantiate express disease-related claims was reasonable. *POM Wonderful, LLC v. FTC*, No. 13-1060, slip op. (D.C. Cir. Jan. 30, 2015). The court observed that several FTC consent orders over the past decade "require *only* 'competent and reliable scientific evidence'—not necessarily RCTs, let alone two RCTs" to substantiate claims, and that FTC "precedents suggest that two-RCT remedial provisions are only selectively imposed in *specific circumstances* based on *particular concerns*." *Id*. at 43 (emphasis added). Based in part on this history, the court upheld FTC's requirement that the petitioner substantiate its disease claims with at least one

RCT, but determined that FTC could not justify an across-the-board two-RCT requirement for all disease claims. *Id*. at 45.

The claims that the court considered in *POM Wonderful* were deemed disease claims, including claims that the products could treat, prevent, or reduce the risk of heart disease, prostate cancer, and erectile dysfunction, among other conditions. *Id*. at 2. In that case, the court concluded that a single RCT, that was not even required to include all of the "required elements" that the government seeks to impose in the instant case, could be sufficient to substantiate those disease claims. Here, the government seeks to require a more stringent substantiation standard – RCTs conducted on the exact product/probiotic strains in the target population (healthy people) – for non-disease, digestive health benefit claims than the standard that the court in *POM Wonderful* determined was reasonable for the substantiation of disease claims. This represents a novel and unprecedented legal standard for the substantiation of non-disease claims that, according to Dr. Laine, would be mandatory for *all* dietary supplements, as discussed further below.

II. The Government's Newly-Asserted General Substantiation Standard, if Upheld, Would Have a Significant Impact on the Entire Dietary Supplement Industry

The government's assertion in its response to CRN's October *Amicus* Brief that this case is "not about a change to a legal standard or an attempt by the government to re-make the dietary supplement industry," but is instead solely

about the substantiation for the specific PCH claims, Dkt. No. 40 at 1, is belied by the testimony of the government's expert, Dr. Laine.

A. Dr. Laine Would Impose His Drug-Like RCT Requirement on All Dietary Supplement Claims

In his deposition, Dr. Laine explained that his substantiation standard, summarized above, was not specifically tailored to Bayer's claims for PCH based upon his expertise in gastroenterology – the field the FTC asserted was the relevant expertise in this case (Dkt. No. 4 at 16) – but rather that it "would be a general rule . . . [i]t's not GI-based." Dkt. No. 73-2 at 128:21-22. Dr. Laine asserts that his standard applies regardless of whether the products are "dietary supplements or drugs," Dkt. No. 73-2 at 229:15-21, and is necessary in order to produce accurate, reliable estimates of outcomes in clinical research for *any* intervention – from drugs and dietary supplements to physical therapy and dietary modifications. *See, e.g.*, *id*. at 128:1-14 ("It can be a supplement. It could be a medication. Where . . . you're doing clinical research, you're not looking at whether it is a drug, a food, et cetera.); 131:1-12 ("[T]his is any intervention . . . if you're talking about getting accurate, . . . reliable results, how could it be different for anything?"); 55:2-11 ("I developed a test that I think everybody would agree who does clinical research would be most likely to . . . produce reliable and accurate results . . . [i]n any situation. So it doesn't matter -- it's not for a drug or probiotic. It's not for FDA or FTC. It's really for a clinical trial . . . to produce . . . valid and reliable results.")

In sum, according to Dr. Laine, RCTs effectively would be required to substantiate *every* health benefit claim, for he testified that "placebo-controlled, double-blind randomized *is the norm* . . . [that is] [w]idely accepted by [his] partners in evidence-based medicine, widely accepted by authors, widely accepted by people who do clinical research as what *the appropriate way to get valid, accurate, reliable results*." *Id.* at 127:8-20 (emphasis added).

Dr. Laine thus has articulated a standard not for the substantiation of Bayer's digestive health benefit claims for PCH, as the government has represented, but rather for the conduct of clinical research. But this case is not about how clinical researchers conduct their studies. It is about what constitutes "competent and reliable scientific evidence" for the specific non-disease digestive health benefit claims Bayer made for PCH. Dr. Laine's standard for how to conduct clinical research is irrelevant to the question at hand.

B. Dr. Laine Would Find Virtually an Entire Industry Sector's Claims Unsubstantiated

Of particular concern to CRN is that Dr. Laine expressly discussed a number of marketed probiotic dietary supplement products making non-disease digestive health benefit claims similar to those Bayer makes for PCH. He testified that all such non-disease claims for these products would need to be substantiated under his standard of RCTs examining the specific strain or combination of strains in the products in the target population to which the products are marketed (*i.e.*, healthy

people). *See, e.g.*, *id*. at 291:10-21 (regarding claim to "protect against episodic gas and bloating" for Align); *id.* at 300:21-301:10 (regarding claims of "helps with occasional diarrhea" and "helps with gas and bloating" for Culturelle); *id.* at 304:4-18 (regarding claim of "daily protection against occasional gas, bloating, constipation" for Pearls Probiotics); *id.* at 307:3-15 (regarding claim of "patented strain to alleviate occasional gas and bloating" for Nature's Bounty); *id.* at 308:7-19 (regarding claim of "helps prevent occasional gas and bloating" for Purelife Naturals). Dr. Laine testified that he was not aware of any high quality study meeting his study design for any of these probiotic products. *Id*. at 311:1-18.

C. Dr. Laine's Substantiation Standard is Aberrational and Inappropriate for Non-Disease Claims for Probiotic Supplements

Dr. Laine's standard is aberrational and inappropriate for non-disease claims for probiotics in particular and dietary supplements in general. Dr. Laine admitted he is not an expert in probiotics, nor has he ever conducted any clinical trial or other study of any kind on probiotics. *See, e.g.*, *id*. at 299:21-22 ("I am not an expert in probiotics, nor did I claim to be."); *id.* at 381:10-15. By contrast, Bayer proffered experts in probiotics and the conduct of research for dietary supplements. These experts explained that clinical trials of the type required by Dr. Laine are neither necessary nor appropriate for non-disease digestive health benefit claims about probiotics.

For example, Bayer expert Dr. Daniel Merenstein, a physician who has conducted clinical trials and other studies on probiotics, explained in his declaration that "experts from a variety of disciplines and countries agree that strain specificity and drug-level randomized controlled trials are not required" for general health benefit claims for the species of bacteria in PCH. Dkt. No. 73-4 at 9. Likewise, Bayer expert Dr. Jeffrey Blumberg, who is experienced in conducting clinical trials for dietary supplements, confirmed in his declaration that his scientific and academic colleagues "do not require or expect RCTs on dietary supplements," Dkt. No. 73-6 at 13, as they are "not the best method by which to reveal the role of nutrients and dietary constituents in healthy people." *Id.* at 2. Rather, Dr. Blumberg affirmed that "competent and reliable scientific evidence" for non-disease claims for dietary supplements "can be obtained from the totality of several well-established research approaches, including *in vitro* experiments, animal models, population-based cohorts (observational research), and clinical trials, including but not limited to RCTs." *Id.* at 5.

Bayer's experts agree with Dr. Laine that none of the claims for the probiotic dietary supplements discussed above meet Dr. Laine's drug-like substantiation standard. *See, e.g.*, Dkt. No. 73-4 at 11 (Dr. Merenstein Declaration stating that he knows of no probiotic that meets Dr. Laine's standard); Dkt. No. 73-3 at 4-5 (Dr. Brian Fennerty Declaration stating that he is aware that none of these

probiotic products are supported by drug-type clinical trials that would meet the government's test articulated in this case). These experts believe Dr. Laine's standard is not only inappropriate in this case, but also could bring the dietary supplement industry to a grinding halt. *See, e.g.*, Dkt. No. 73-6 at 13 (Dr. Blumberg Declaration stating, "If Dr. Laine's drug-level RCT criteria became the law, it would effectively remove almost all of the existing dietary supplements with structure/function claims from the market."); Dkt. No. 73-4 at 11 (Dr. Merenstein Declaration stating, "If Dr. Laine's tests were required for probiotics and supplements, it would likely require nearly all supplement advertising to be eliminated, greatly impacting public health."). Again, such an outcome is precisely what DSHEA was enacted to prevent.

D. Meeting the Government's Substantiation Standard Would Be Inordinately Expensive and Unduly Burdensome

The government's substantiation standard, as articulated by Dr. Laine, would be inordinately expensive and unduly burdensome for dietary supplement marketers making non-disease health benefit claims. At least one, if not more, RCTs would need to be conducted for each particular product formulation and in the target population for which the product is intended – typically healthy individuals. A clinical study containing all of these "required elements" is incredibly expensive to conduct and imposes a significant administrative burden on the study's sponsor. *See, e.g.*, Aylin Sertkaya et al., *Examination of Clinical Trial*

Costs and Barriers for Drug Development (July 25, 2014) at 3-3, *available at* http://aspe.hhs.gov/sp/reports/2014/ClinicalTrials/rpt_erg.pdf (estimating that the cost of conducting an RCT in the gastrointestinal therapeutic area ranges from $14.5 to $15.8 million and that the cost of conducting an RCT in any therapeutic area ranges from $7.0 to $52.9 million).

The requirement that an RCT must be conducted in healthy people would be particularly costly, as it can take years and a very large number of subjects to demonstrate that people who are already healthy and symptom-free will remain that way when using a dietary supplement. For this reason, dietary supplement marketers often examine the effect of a product or dietary ingredient on a slightly-impaired but otherwise healthy population, and then extrapolate from such a study to healthy consumers, based upon bridging evidence such as an understanding of the mechanism of action of the dietary supplement or ingredient. Mechanism of action data may help substantiate a claim that the product or ingredient that benefits the impaired study population will maintain health in an already-healthy population. FTC has expressly acknowledged that such extrapolation may be reasonable. FTC Guidance at 17.

And of course, it would be incredibly costly to test each particular product formulation, and it is often not necessary to do so where there is no scientific basis to believe that ingredients in combination will act differently than when

administered separately. In the case of probiotics, where the relevant expert scientific community has determined that species-specific data are sufficient to support a claim, it may not be necessary to test the particular strain, as detailed in Bayer's Response Brief. *See, e.g.*, Dkt. No. 74 at 26 n.10. Requiring costly product-specific RCTs in healthy populations is therefore unjustified as a general rule for non-disease, health benefit claims for dietary supplements. Moreover, such a standard is comparable to that required for FDA approval of new drugs, but unlike drug companies, dietary supplement companies obtain no market exclusivity and typically secure no patent protection through which they might recoup their research investment.

Historically, in considering whether evidence is sufficient to substantiate a claim, the FTC has considered a number of factors, which include the type of claim, the consequences of a false claim, the benefits of a truthful claim, and the cost of developing substantiation for the claim. *See, e.g.*, Policy Statement Regarding Advertising Substantiation Program, *appended to Thompson Med. Co.*, 104 F.T.C. 648, 839-840 (1984), *aff'd*, 791 F.2d 189 (D.C. Cir. 1986). FTC has traditionally considered these factors on a case-by-case basis so as to account for the specific characteristics of a particular product and its target population. Balancing these factors, including the cost of substantiating a claim, is particularly important when evaluating the substantiation for non-disease, health benefit claims

for dietary supplements, given Congress' clearly expressed intent to distinguish dietary supplements from drugs, to provide for the dissemination of truthful and informative information about the benefits of dietary supplements to consumers, and to limit unreasonable regulatory barriers that would prevent the commercial flow of safe dietary supplement products. Imposing a rigid and unnecessarily costly across-the-board drug-like RCT requirement on the dietary supplement industry would depart entirely from the balancing test that FTC has acknowledged as critical in the past and would indeed prevent the flow of safe dietary supplement products, and scientifically valid and informative information about those products, to consumers.

E. The Government Untenably Asserts that its Standard is Uniquely Tailored to Bayer While Also Claiming it has Long Required RCTs More Generally

While the government has asserted that the substantiation standard it is applying in this case does not have broad implications for the dietary supplement industry beyond the instant action, in its discovery responses the government has also attempted to demonstrate that its proposed substantiation standard is not new and could be applied in a broader context. Specifically, when the government was asked in discovery requests to identify all occasions when the United States publicly asserted that "competent and reliable scientific evidence" requires clinical trials meeting Dr. Laine's study design, the government produced two charts

identifying instances when the government "has asserted with varying degrees of specificity the need for a randomized clinical trial to support a performance, benefits, or efficacy claim relating to dietary supplements." Dkt. No. 73-9 at 9; *see also* Dkt. No. 73-10.

The government appears to be trying to straddle both sides of the fence. On the one hand, it asserts that the substantiation standard proffered in the instant action is tailored specifically to Bayer's particular claims for PCH and does not represent a general standard for the broader dietary supplement industry. On the other hand, the government defends its standard in this case as not new because it allegedly has been announced publicly in a variety of contexts. This approach is further undermined by the fact that most of the items on these charts were not even in the public domain, as detailed in Bayer's Response Brief. Dkt. No. 74 at 35. Further, many of the examples that the government provided of past assertions of the need for RCTs to substantiate dietary supplement claims were speeches by FTC employees that reflected those employees' individual views, and not the views of the FTC or any individual Commissioner. *See* Dkt. No. 73-10. Other examples included consent decrees that expressly required RCTs to substantiate certain dietary supplement claims. *See* Dkt. No. 73-9. Such consent decrees reflect only the agreement of the parties to settle a particular case, and as FTC officials have often stated, provisions in consent decrees are not considered agency

guidance for industry more broadly. *See, e.g.*, Statement of Chairwoman Edith Ramirez and Commissioner Julie Brill In the Matter of GeneLink, Inc. and foru International Corporation (Jan. 7, 2014) at 2-3, *available at* http://www.ftc.gov/public-statements/2014/01/statement-chairwoman-edith-ramirez-commissioner-julie-brill.

The government could not provide any examples of instances in which it has officially expressed, broadly, that "competent and reliable scientific evidence" must include RCTs with all of the "required elements" now demanded, because the government has never articulated this position in the past. Instead, as described in detail above, the government has consistently communicated that "competent and reliable scientific evidence" can include a wide range of scientific studies. The FTC has put neither Bayer nor the broader dietary supplement industry on notice that randomized, placebo-controlled, double-blind human clinical studies conducted on the actual product bearing the claim and in the target population for the product, *i.e.*, healthy consumers, would be required for all dietary supplement non-disease health benefit claims. As detailed in the following Section, the government must not be permitted to impose such a standard retroactively through a contempt proceeding.

III. The Government Must Provide Clear and Consistent Guidance to the Dietary Supplement Industry About Substantiation and Cannot Change the Standard Retroactively Through Individual Enforcement Actions

As discussed in depth in CRN's October *Amicus* Brief, the dietary supplement industry has for years relied upon guidance issued by FTC and FDA in determining how to substantiate claims made about dietary supplement products. These guidance documents communicate principles that apply across the industry and are the only general public communication of the government's current thinking about substantiation – which is an approach that allows for substantial flexibility in substantiating claims made in dietary supplement advertising and labeling. The government has not communicated publicly any intent to depart from the concepts articulated in that agency guidance. The FTC has not withdrawn its guidance, nor has it undertaken rulemaking or other agency action to further clarify, in a broad manner, what types of evidence can be used to substantiate dietary supplement claims. Instead, through the instant contempt action, the government is attempting to significantly narrow its previously communicated substantiation standard with no prior notice to industry. This is procedurally improper and could have a chilling effect on the entire supplement industry. Particularly under the FTC regulatory regime, in which the FTC typically does not send warning letters giving companies an opportunity to cure but rather proceeds with enforcement actions, the FTC must clearly and publicly articulate the substantiation standard to which dietary supplement marketers will be held.

In the instant action, the FTC has departed from its longstanding flexible criteria for the substantiation of claims made for dietary supplements based on the opinion of a single expert. That expert has concluded that, as a general rule, "competent and reliable scientific evidence" must always include drug-like RCTs examining the specific formulation in the target population for the product. This conclusion is not limited to the PCH product, nor is it limited to products making digestive health-related claims; instead, Dr. Laine asserts that RCTs with all of the "required elements" are necessary to substantiate claims for any health-related intervention.

Departing from previously articulated criteria, retroactively, through a contempt action creates a moving target for the substantiation of dietary supplement claims with which it would be impossible to comply. The government cannot redefine the substantiation standard through a contempt action. *See, e.g.*, *Basic Research, LLC v. FTC*, No. 2:09-cv-0779, 2014 U.S. Dist. LEXIS 169043, at *43 (D. Utah Nov. 25, 2014) (rejecting the FTC's asserted substantiation standard because it exceeded the requirements of the consent order); *FTC v. Garden of Life, Inc.*, 845 F. Supp. 2d 1328, 1335 (S.D. Fla. 2012), *aff'd in part and vacated and remanded in part*, 516 F. App'x 852 (11th Cir. 2013) (declining to adopt FTC's asserted substantiation standard because it would require the court to "read additional requirements into the Consent Decree"). Further, implicit in the

government's role in ensuring that claims are adequately substantiated "is the expectation of reasonableness." *Basic Research* at *43; *see also POM Wonderful* at 44-45 (holding that the FTC's asserted across-the-board two-RCT requirement was not "reasonably linked" to government's interest in preventing deceptive speech). To allow otherwise would enable the government to take enforcement action without putting dietary supplement manufacturers on notice of the substantiation standard expected when developing and substantiating claims.

In addition, as discussed in detail in CRN's October *Amicus* brief, limiting the scope of substantiating evidence to only RCTs containing all of the "required elements" would halt the flow of truthful, non-misleading, valuable, and scientifically sound information about the health benefits of dietary supplements. Dkt. No. 24-2 at 17-19. By asserting that "competent and reliable scientific evidence" must consist of RCTs with all of the "required elements," without any previous notice, and by making clear that this new standard would apply to all non-disease health benefit claims made about dietary supplements, the government's standard for substantiation would impinge upon the First Amendment rights of all dietary supplement marketers.

If the government prevails in holding Bayer to the substantiation standard it seeks to impose, there would be significant ramifications for the dietary supplement industry and for consumers. The standard the government seeks to

impose here would cause confusion about the regulatory regime that would apply to a given product or a given claim, and the dietary supplement industry would not know whether it could rely on established FTC guidance articulating a flexible substantiation standard or whether it could be held to a more rigid substantiation standard through an FTC enforcement action. Without clear and consistent guidance from the government regarding the substantiation standard for dietary supplement claims, dietary supplement companies would likely refrain from providing truthful, valuable, and scientifically sound information about dietary supplement products to consumers out of fear of enforcement action premised on the narrow substantiation standard articulated in this case. This would limit consumers' ability to make fully informed nutrition-related decisions, which is clearly contrary to Congress's intent.

CONCLUSION

CRN does not take a position on any scientific or factual issues in this case. However, in reaching a decision, CRN urges the Court to reject the government's novel legal standard for the substantiation of dietary supplement claims that contravenes Congressional intent and departs from longstanding agency guidance and industry practice. Instead, CRN submits, the Court should evaluate the contempt action under the longstanding, flexible substantiation standard upon which the entire dietary supplement industry relies. In the event the court finds the

government's substantiation standard to be appropriate in this particular case, CRN requests that the court do so on narrow and clearly-articulated grounds that demonstrate this rigid and strict substantiation standard applies only to the Bayer product and claims at issue in this contempt action. To allow otherwise would have a chilling effect throughout the dietary supplement industry and would significantly limit the ability of industry to share with consumers truthful and scientifically valid information about its products.

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Respectfully submitted,

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